OraQuick® ADVANCE

Rapid HIV-1/2 Antibody Test

Read this package insert completely before using the product. Follow the instructions carefully when performing testing. Not doing so may result in inaccurate test results. Before performing testing, all operators MUST read and become familiar with Universal Precautions for Prevention of Transmission of Human Immunodeficieny Virus, Hepatitis B Virus, and other Blood-borne Pathogens in Health-Care Settings.[5]

COMPLEXITY: WAIVED

for Oral Fluid, Fingerstick Whole Blood and Venipuncture Whole Blood. Any modification by the laboratory to the test system or FDA approved test system instructions will result in the test no longer meeting the requirements for waived category.

COMPLEXITY: MODERATE

for Plasma.

NAME AND INTENDED USE

The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test is a single-use, qualitative immunoassay to detect antibodies to Human Immunodeficiency Virus Type 1 (HIV-1) and Type 2 (HIV-2) in oral fluid, fingerstick whole blood, venipuncture whole blood and plasma specimens. The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test is intended for use as a point-of-care test to aid in the diagnosis of infection with HIV-1 and HIV-2. This test is suitable for use in multi-test algorithms designed for statistical validation of rapid HIV test results. When multiple rapid HIV tests are available, this test should be used in appropriate multi-test algorithms.

RESTRICTIONS

- **Sale of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test is restricted to clinical laboratories**
  - **that have an adequate quality assurance program, including planned systematic activities to provide adequate confidence that requirements for quality will be met; and**
  - **where there is assurance that operators will receive and use the instructional materials.**
- **The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test is approved for use only by an agent of a clinical laboratory.**
- **Test subjects must receive the "Subject Information" pamphlet prior to specimen collection and appropriate information when test results are provided.**
- **The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test is not approved for use to screen blood or tissue donors.**

SUMMARY AND EXPLANATION OF THE TEST

Acquired Immune Deficiency Syndrome (AIDS), AIDS related complex (ARC) and pre-AIDS are thought to be caused by the Human Immunodeficiency Virus (HIV). The first AIDS-related virus, HIV-1 (also known as HTLV-III, LAV-1 and ARV) has been isolated from patients with AIDS and from healthy persons at high risk for AIDS.[1,2] Genetic analysis of HIV-1 isolates has documented the existence of subtypes. To date, eight HIV-1 subtypes (A through H), designated as Group M, have been identified world-wide in addition to the highly divergent HIV-1 isolates from AIDS patients in Cameroon, designated as Group O.[3] A closely related but distinct second type of pathogenic human immunodeficiency retrovirus, designated HIV-2 (formerly LAV-2), has been isolated from West African patients with AIDS. HIV-2 has been shown to share a number of conserved sequences with HIV-1, but serological cross-reactivity between HIV-1 and HIV-2 has been shown to be highly variable from sample to sample.

HIV is known to be transmitted by sexual contact, by exposure to blood (including sharing contaminated needles and syringes) or by contaminated blood products, or it may be transmitted from an infected mother to her fetus during the prenatal period. Individuals infected with HIV produce antibodies against the HIV viral proteins. Testing for the presence of antibodies to HIV in bodily fluids (e.g., blood, oral fluid, and urine) is an accurate aid in the diagnosis of HIV infection. However, the implications of seropositivity must be considered in a clinical context. For example, in neonates, the presence of antibodies to HIV is indicative of exposure to HIV, but not necessarily of HIV infection, due to the acquisition of maternal antibodies that may persist for up to eighteen months. Conversely, absence of antibody to HIV cannot be taken as absolute proof that an individual is free of HIV infection or incapable of transmitting the virus. An antibody response to a recent exposure may take several months to reach detectable levels. HIV has been isolated from asymptomatic, seronegative individuals presumably before seroconversion following exposure.

The standard laboratory HIV testing algorithm used in the United States consists of screening with an enzyme immunoassay (EIA) and confirmation of repeatedly reactive EIAs using a Western blot test. Results are typically reported within 48 hours to 2 weeks, making these standard screening and supplemental tests inadequate to meet the need for rapid HIV diagnosis. The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test is a point-of-care test to aid in the diagnosis of infection with HIV-1 and HIV-2.

Using a rapid HIV test increases the number of HIV-infected persons who may be diagnosed. The Centers for Disease Control and Prevention (CDC) estimates that nearly one third of the estimated 900,000 HIV-infected persons in the United States do not know their HIV status. As a result, they cannot benefit from early intervention with effective antiviral therapy. Rapid HIV testing addresses this

issue by providing results during the initial visit and enabling immediate counseling. Additionally, for pregnant women who do not know their HIV status at the time of delivery, rapid HIV testing permits therapy to be initiated for these mothers during labor, and to their infants post partum, substantially reducing the chance that the infants will become infected with HIV. Likewise, rapid HIV testing is instrumental in the decision to initiate treatment for health care workers after accidental exposures to body fluids from infected individuals. In the U.S., it is estimated that 600,000 to 1,000,000 "needlestick injuries" occur each year. Critical decisions about treatment depend on the availability of accurate, rapid HIV test results.

BIOLOGICAL PRINCIPLES OF THE TEST

The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test is a manually performed, visually read, 20 minute immunoassay for the qualitative detection of antibodies to HIV-1 and HIV-2 in human oral fluid, whole blood obtained from a finger puncture or a venipuncture, and plasma. The OraQuick® *ADVANCE* rapid test is comprised of a single-use test device and a single-use vial containing a pre-measured amount of a buffered developer solution. Each component is sealed in separate compartments of a single pouch to form the test. The OraQuick® *ADVANCE* rapid test utilizes a proprietary lateral flow immunoassay procedure. The device plastic housing holds an assay test strip comprised of several materials that provide the matrix for the immunochromatography of the specimen and the platform for indication of the test results.

The assay test strip, which can be viewed through the test device result window, contains synthetic peptides representing the HIV envelope region and a goat anti-human IgG procedural control immobilized onto a nitrocellulose membrane in the Test (T) zone and the Control (C) zone, respectively.

An oral fluid specimen is collected using the flat pad on the test device, followed by the insertion of the test device into the vial of developer solution. A fingerstick whole blood, venipuncture whole blood or plasma specimen is collected and transferred into the vial of developer solution, followed by the insertion of the test device. The developer solution facilitates the flow of the specimen into the device and onto the test strip. As the diluted specimen flows through the device, it rehydrates the protein-A gold colorimetric reagent contained in the device. As the specimen continues to migrate up the strip, it encounters the T zone. If the specimen contains antibodies that react with the antigens immobilized on the nitrocellulose membrane, a reddish-purple line will appear, qualitatively indicating the presence of antibodies to HIV-1 and/or HIV-2 in the specimen. The intensity of the line color is not directly proportional to the amount of antibody present in the specimen.

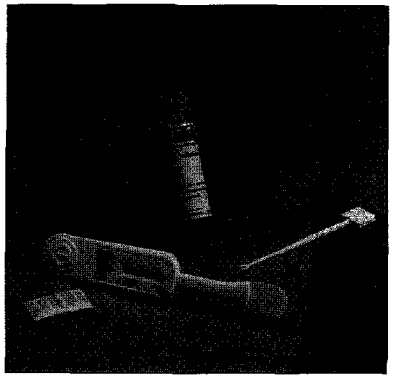
Further up the assay strip, the sample will encounter the C zone. This built-in procedural control serves to demonstrate that a specimen was added to the vial and that the fluid has migrated adequately through the test device. A reddish-purple line will appear in the C zone during the performance of all valid tests, whether or not the sample is positive or negative for antibodies to HIV-1 and/or HIV-2 (refer to the *Test Result and Interpretation of Test Result* section below).

The test results are interpreted after 20 minutes but not more than 40 minutes after the introduction of the test device into the developer solution containing the test specimen. No precision pipeting, predilutions, or specialized instrumentation are required to perform the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test.

MATERIALS PROVIDED

OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test Kits are available in the following packaging configurations:

Kit Size	100 Count	25 Count
Divided Pouches, each containing: Test Device (1) Absorbent Packet (1) Developer Solution Vial (1) (each vial contains 1 mL of a phosphate buffered saline solution containing polymers and an antimicrobial agent)	100	25
Reusable Test Stands	10	5
Specimen Collection Loops	100	25
Subject Information Pamphlets	100	25
Package Insert	1	1
Customer Letter	1	1



MATERIALS REQUIRED AND AVAILABLE AS AN ACCESSORY TO THE KIT

OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test Kit Controls
Package contains HIV-1 Positive Control (1 vial, black cap, 0.2 mL), HIV-2 Positive Control (1 vial, red cap, 0.2 mL) and Negative Control (1 vial, white cap, 0.2 mL), and a Package Insert

MATERIALS REQUIRED BUT NOT PROVIDED

Timer or watch capable of timing 20 to 40 minutes
Clean, disposable, absorbent workspace cover
Biohazard waste container
Additional items required for fingerstick and venipuncture whole blood collection, and plasma specimens:
Antiseptic wipe
Sterile lancet to obtain a fingerstick whole blood specimen, or materials required to obtain a venipuncture whole blood specimen
Sterile gauze pads
Latex, vinyl or nitrile disposable gloves (optional for oral fluid testing)
Centrifuge to process a plasma specimen

WARNINGS

For *in vitro* Diagnostic Use

1. **Read the package insert completely before using the product. Follow the instructions carefully. Not doing so may result in inaccurate test results.**
2. **Before performing testing, all operators MUST read and become familiar with Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and other Blood-borne Pathogens in Health-Care Settings.[5]**
3. **FOA has approved this kit for use with oral fluid, fingerstick whole blood, venipuncture whole blood, and plasma specimens only. Use of this test kit with specimen types other than those specifically approved for use with this device may result in inaccurate test results.**
4. **This test should be performed at temperatures in the range of (15°- 37°C, 59°- 99°F). If stored refrigerated, ensure that the Divided Pouch is brought to operating temperature (15°- 37°C, 59°- 99°F) before performing testing.**
5. **If the test kit is stored at temperatures outside of ambient temperature (15°- 27°C, 59°- 80°F), or used outside of the operating temperature (15°- 37°C, 59°- 99°F), use the Kit Controls to ensure performance of the test.**
6. **Individuals infected with HIV-1 and/or HIV-2 who are receiving highly active antiretroviral therapy (HAART) may produce false negative results.**

PRECAUTIONS

Safety Precautions

1. Handle blood specimens and materials contacting blood specimens as if capable of transmitting infectious agents.
2. Do not drink, eat, or smoke in areas where specimens are being handled or testing is being performed.
3. Wear disposable gloves while handling blood specimens and performing testing of blood specimens. Change gloves and wash hands thoroughly after performing each test. Dispose of used gloves in a biohazard waste container.
4. Oral fluid is not considered potentially infectious unless it contains blood.[8] Use of gloves for oral fluid testing is optional. Test administrators with breaks in the skin (cuts, abrasions, or dermatitis) should wear gloves when performing oral fluid testing. Wash hands thoroughly after performing each oral fluid test and after contact with oral fluid.
5. Dispose of all test specimens and materials used in the test procedure in a biohazard waste container. Lancets and venipuncture materials should be placed in a puncture-resistant container prior to disposal. The recommended method of disposal of biohazard waste is autoclaving for a minimum of 1 hour at 121°C. Disposable materials may be incinerated. Liquid wastes may be mixed with appropriate chemical disinfectants. A freshly prepared solution of 10% bleach (0.5% solution of sodium hypochlorite) is recommended. Allow 60 minutes for effective decontamination. **NOTE: Do not autoclave solutions that contain bleach.**
6. Wipe all spills thoroughly with a solution of 10% bleach or other appropriate disinfectant[4]. Bleach solutions should be made fresh each day.
7. For additional information on biosafety, refer to "Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and other Blood-borne Pathogens in Health-Care Settings" [5] and "Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis".[8]

Handling Precautions

1. Use all Specimen Collection Loops, Test Devices, and Developer Solution Vials only once and dispose of properly (see Safety Precautions). **Do not reuse any of these test components.**
2. Do not use the test beyond the expiration date printed on the Divided Pouch. Always check expiration date prior to testing.
3. Do not interchange Test Devices and Developer Solution Vials from kits with different lot numbers.
4. Avoid microbial contamination and exercise care in handling the kit components.
5. To ensure accurate results, the Test Device must be inserted into the Developer Solution Vial within 60 minutes after introducing the fingerstick whole blood, venipuncture whole blood or plasma sample.
6. When collecting oral fluid specimens the Test Device must be inserted into the Developer Solution Vial within 10 minutes of collection.
7. Adequate lighting is required to read a test result.

STORAGE INSTRUCTIONS

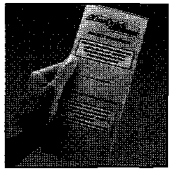
Store unused OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Tests unopened at 2°-27°C (35°-80°F). Do not open the Divided Pouch until you are ready to perform a test. If stored refrigerated, ensure that the Divided Pouch is brought to operating temperature (15°- 37°C, 59°- 99°F) before opening.

DIRECTIONS FOR USE

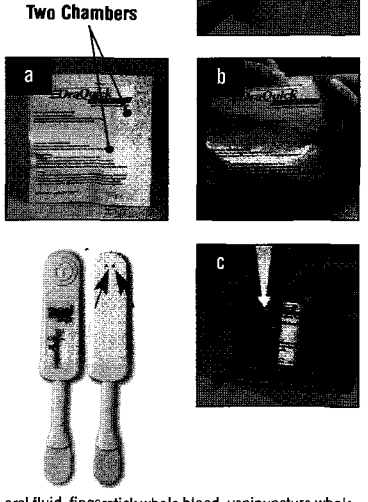
SET UP YOUR WORKSPACE

- Gather the materials you will need.
- Allow the test kit to come to operating temperature (15°- 37°C; 59°- 99°F) before use.
- Refer to the *External Quality Control* section in this package insert to determine when the Kit Controls should be run.
- Cover your workspace with a clean, disposable, absorbent workspace cover.
- Set an OraQuick® *ADVANCE* Reusable-Test Stand ("Stand") up on your workspace cover. Use only the stand provided.
- Put on your disposable gloves as required in accordance with the *Safety Precautions* section in this package insert.

Prior to testing provide the "Subject Information" pamphlet to the person being tested.



GENERAL TEST PREPARATION



1. Open the two chambers of the OraQuick® *ADVANCE* Divided Pouch ("Pouch") by tearing at the notches on the top of each side of the Pouch (*see picture a and b*). To prevent contamination, leave the Test Device ("Device") in the Pouch until you are ready to use it.
2. Remove the Developer Solution Vial ("Vial") from the Pouch. Hold the Vial firmly in your hand. Carefully remove the cap from the Vial by gently rocking the cap back and forth while pulling it off. Set the cap on your workspace cover.
3. Slide the Vial into the top of one of the slots in the Stand. **DO NOT** force the vial into the Stand from the front of the slot as splashing may occur. Make sure the Vial is pushed all the way to the bottom of the slot in the stand (*see picture c*).

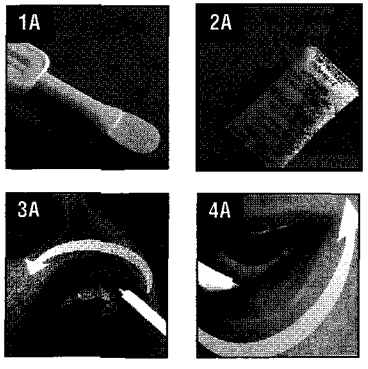
NOTE: DO NOT cover the two holes in the back of the Device with labels or other materials. Doing so may cause an Invalid result.

SPECIMEN COLLECTION AND TESTING PROCEDURE

The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test can be used for testing oral fluid, fingerstick whole blood, venipuncture whole blood, and plasma specimens. Refer to the specific testing procedure below.

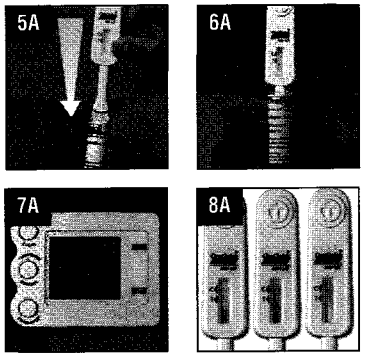
ORAL FLUID PROCEDURE

STEP 1: COLLECT



1. Have the person being tested remove the Device from its Pouch. **DO NOT** allow the person to touch the Flat Pad (*see picture 1A*). Check to make sure that an Absorbent Packet is included with the Device (*see picture 2A*). If no Absorbent Packet is present, discard the Device and obtain a new Pouch for testing.
2. Direct the person to place the Flat Pad above the teeth against the outer gum. Direct the person to gently swab completely around the outer gums, both upper and lower, one time around, using the Flat Pad (*see pictures 3A and 4A*). **DO NOT** allow the person to swab the roof of the mouth, the inside of the cheek or the tongue. **NOTE:** Both sides of the Flat Pad may be used during this procedure.

STEP 2: TEST



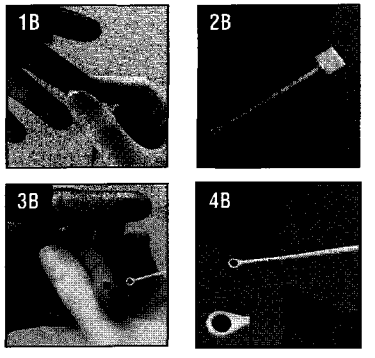
1. Instruct the person being tested to insert the Flat Pad of the Device all the way into the Vial (*see picture 5A*). Make sure that the Flat Pad touches the bottom of the Vial. The Result Window on the Device should be facing towards you (*see picture 6A*).
2. Start timing the test (*see picture 7A*). **DO NOT** remove the Device from the Vial while the test is running. Pink fluid will appear and travel up the Result Window. The pink fluid will gradually disappear as the test develops (*see picture 8 A*). Read the results after 20 minutes but not more than 40 minutes in a fully lighted area.
3. Refer to the *Test Result and Interpretation of Test Result* section in this package insert.

FINGERSTICK WHOLE BLOOD AND VENIPUNCTURE WHOLE BLOOD PROCEDURE

STEP 1: COLLECT

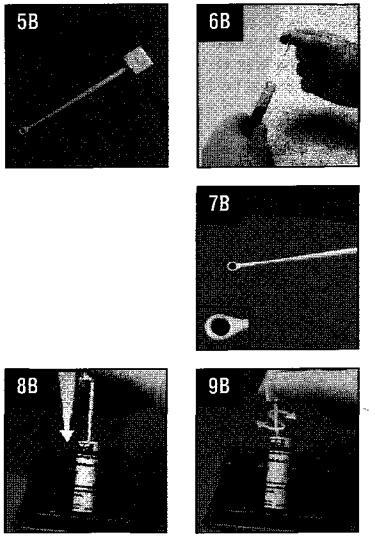
Whole blood specimens may be collected either by fingerstick (*see Step 1.A*) or by venipuncture (*see Step 1.B*).

STEP 1.A: FINGERSTICK WHOLE BLOOD



1. Using an antiseptic wipe, clean the finger of the person being tested. Allow the finger to dry thoroughly or wipe dry with a sterile gauze pad. Using a sterile lancet, puncture the skin just off the center of the finger pad. Hold the finger downward. Apply gentle pressure beside the point of the puncture. Avoid squeezing the finger to make it bleed (*see picture 1B*). Wipe away this first drop of blood with a sterile gauze pad. Allow a new drop of blood to form.
2. Pick up an unused Specimen Collection Loop ("Loop") by the thick "handle" end (*see picture 2B*). Put the "rounded" end of the Loop on the drop of blood (*see picture 3B*). Make sure that the Loop is completely filled with blood (*see picture 4B*). NOTE: If the Loop is dropped or comes in contact with any other surface, discard it in a biohazard waste container. Get a new Loop for the collection of the blood sample.

STEP 1.B: VENIPUNCTURE WHOLE BLOOD



1. Using standard venous phlebotomy procedures, collect a whole blood sample using a tube containing any of the following anticoagulants: EDTA (lavender top), sodium heparin (green top), sodium citrate (light blue top), or ACD Solution A (yellow top). **Other anticoagulants have not been tested and may give an incorrect result.** If the specimens are not tested at the time of collection, the whole blood may be stored at 2°-18°C (35°-64°F) for up to 30 hours. Prior to testing, mix the blood tube gently by inversion several times to ensure a homogeneous sample.
2. Pick up an unused Specimen Collection Loop ("Loop") by the thick "handle" end (*see picture 5B*). Put the "rounded" end of the Loop into the tube of blood (*see picture 6B*). Make sure that the Loop is completely filled with blood (*see picture 7B*). NOTE: If the Loop is dropped or comes in contact with any other surface, discard it in a biohazard waste container. Get a new Loop for the collection of the blood sample.

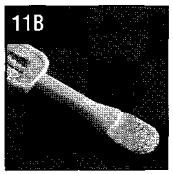
STEP 2: MIX

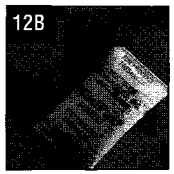
1. Immediately insert the blood-filled end of the Loop all the way into the Vial (*see picture 8B*). Use the Loop to stir the blood sample in the Developer Solution ("Solution") (*see picture 9B*). Remove the used Loop from the Solution. Throw the used Loop away in a biohazard waste container.

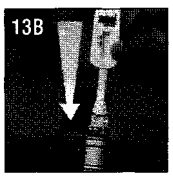
2. Check the Solution to make sure that it appears pink. This means that the blood was correctly mixed into the Solution (*see picture 10B*). If the Solution is not pink, discard all test materials in a biohazard waste container. Start the test over. Use a new Pouch and a new blood sample.

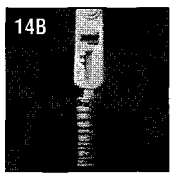
STEP 3: TEST

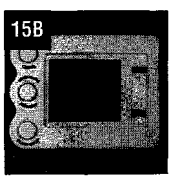
1. Remove the Device from the Pouch. **DO NOT** touch the Flat Pad (*see picture 11B*). Check to make sure that an Absorbent Packet is included with the Device (*see picture 12B*). If no Absorbent Packet is present, discard the Device and obtain a new Pouch for testing.
2. Insert the Flat Pad of the Device all the way into the Vial containing the blood sample (*see picture 13B*). Make sure that the Flat Pad touches the bottom of the Vial. The Result Window on the Device should be facing towards you (*see picture 14B*).
3. Start timing the test (*see picture 15B*). **DO NOT** remove the Device from the Vial while the test is running. Pink fluid will appear and travel up the Result Window. The pink fluid will gradually disappear as the test develops (*see picture 16B*). Read the results after 20 minutes but not more than 40 minutes in a fully lighted area.
4. Refer to the *Test Result and Interpretation of Test Result* section in this package insert.

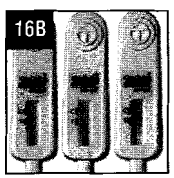










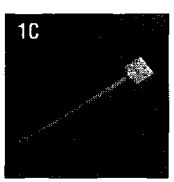


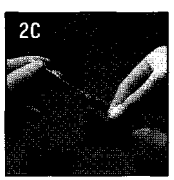
PLASMA PROCEDURE

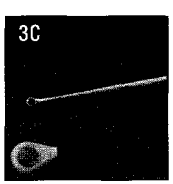
NOTE: Testing of plasma samples may only be performed by laboratories certified to perform Moderate Complexity tests.

STEP 1: COLLECT

1. Using standard venous phlebotomy procedures, collect a whole blood sample using a tube containing EDTA (lavender top) anticoagulant. **Other anticoagulants have not been tested and may give an incorrect result.** If the specimens are not tested at the time of collection, the specimen may be stored as whole blood or plasma for up to 7 days at 2°-8°C (35°-46°F).
2. Centrifuge the tube of blood [1000-1300 x *g*, for approximately 5 minutes, no refrigeration required] to separate the cells from the plasma. Carefully uncap the tube by gently rocking the stopper towards you so that it vents away from you.
3. Pick up an unused Specimen Collection Loop ("Loop") by the thick "handle" end (*see picture 1C*). Put the "rounded" end of the Loop into the tube of plasma (*see picture 2C*). Make sure that the Loop is completely filled with plasma (*see picture 3C*). NOTE: If the Loop is dropped or comes in contact with any other surface, discard it in a biohazard waste container. Get a new Loop for the collection of the plasma sample.

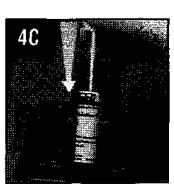


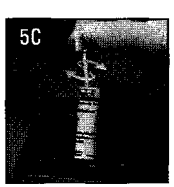




STEP 2: MIX

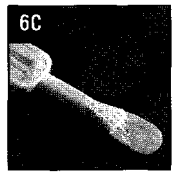
1. Immediately insert the plasma-filled end of the Loop all the way into the Vial (*see picture 4C*). Use the Loop to stir the plasma sample in the Developer Solution ("Solution") (*see picture 5C*). Remove the used Loop from the Solution. Throw the used Loop away in a biohazard waste container.

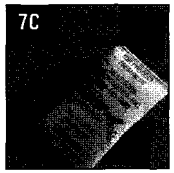


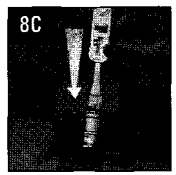


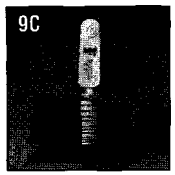
STEP 3: TEST

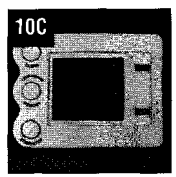
1. Remove the Device from the Pouch. **DO NOT** touch the Flat Pad (*see picture 6C*). Check to make sure that an Absorbent Packet is included with the Device (*see picture 7C*). If no Absorbent Packet is present, discard the Device and obtain a new Pouch for testing.
2. Insert the Flat Pad of the Device all the way into the Vial containing the blood sample (*see picture 8C*). Make sure that the Flat Pad touches the bottom of the Vial. The Result Window on the Device should be facing towards you (*see picture 9C*).
3. Start timing the test (*see picture 10C*). **DO NOT** remove the Device from the Vial while the test is running. Pink fluid will appear and travel up the Result Window. The pink fluid will gradually disappear as the test develops (*see picture 11C*). Read the results after 20 minutes but not more than 40 minutes in a fully lighted area.
4. Refer to the *Test Result and Interpretation of Test Result* section in this package insert.

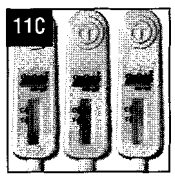












GENERAL TEST CLEAN-UP

1. Dispose of the used test materials in a biohazard waste container.
2. When using gloves, change your gloves between each test to prevent contamination. Throw away the used gloves in a biohazard waste container.
3. Use a freshly prepared 10% solution of bleach to clean up any spills.

QUALITY CONTROL

Built-in Control Features

The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test has a built-in procedural control that demonstrates assay validity. A reddish-purple line in the Control ("C") area of the Result Window indicates that a specimen was added and that the fluid migrated appropriately through the Test Device. The Control line will appear on all valid tests, whether or not the sample is reactive or non-reactive. (Refer to *Test Result and Interpretation of Test Result* section below.)

External Quality Control

OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test Kit Controls are available separately for use only with the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test. The Kit Controls are specifically formulated and manufactured to ensure performance of the Test, and are used to verify your ability to properly perform the test and interpret the results. The HIV-1 and HIV-2 Positive Controls will produce a reactive test result and have been manufactured to produce a very faint Test ("T") line. The Negative Control will produce a non-reactive test result. (Refer to *Test Result and Interpretation of Test Result* section below.) Use of kit control reagents manufactured by any other source may not produce the required results, and therefore, will not meet the requirements for an adequate quality assurance program for the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test.

Run the Kit Controls under the following circumstances:

- **Each new operator prior to performing testing on patient specimens,**
- **When opening a new test kit lot,**
- **Whenever a new shipment of test kits is received,**
- **If the temperature of the test kit storage area falls outside of 2°- 27°C (35°- 80°F),**
- **If the temperature of the testing area falls outside of 15°- 37°C (59°- 99°F), and**
- **At periodic intervals as dictated by the user facility.**

Refer to the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test Kit Controls package insert for instructions on the use of these reagents. It is the responsibility of each laboratory using the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test to establish an adequate quality assurance program to ensure the performance of the device under its specific locations and conditions of use. Contact OraSure Technologies' Customer Service if the Kit Control reagents do not produce the expected results.

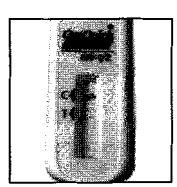
TEST RESULT AND INTERPRETATION OF TEST RESULT

Refer to the Result Window on the Test Device.

NON-REACTIVE

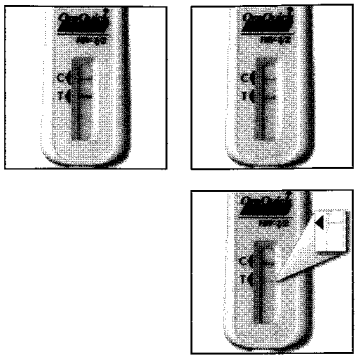
The diagram at the right shows an example of a **Non-Reactive** test result.
A test is Non-Reactive if:

a reddish-purple line appears next to the triangle labeled "C", **and NO** line appears next to the triangle labeled "T".



A **Non-Reactive** test result means that HIV-1 and HIV-2 antibodies were not detected in the specimen. The test result is interpreted as **NEGATIVE for HIV-1 and HIV-2 antibodies**. Follow CDC guidelines to inform the test subject of the test result and its interpretation.[6,7]

REACTIVE
The diagrams at the right show examples of a **Reactive** test result.

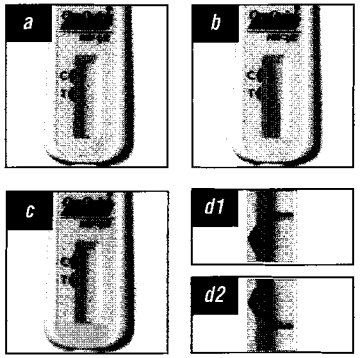


A test is **Reactive** if:
a reddish-purple line appears next to the triangle labeled "C" **and** a reddish-purple line appears next to the triangle labeled "T". One of these lines may be darker than the other.

NOTE: The test is **Reactive** if **any** reddish-purple line appears next to the "T" triangle **and** next to the "C" triangle, no matter how faint these lines are.

A **Reactive** test result means that HIV-1 and/or HIV-2 antibodies have been detected in the specimen. The test result is interpreted as **PRELIMINARY POSITIVE for HIV-1 and/or HIV-2 antibodies.** Follow CDC guidelines to inform the test subject of the test result and its interpretation.[6,7]

INVALID
The diagrams at the right show examples of an **Invalid** test result.



A test is **Invalid** if any of the following occurs:
- **NO** reddish-purple line appears next to the triangle labeled "C" (*see picture a and b*), or
- a red background in the Result Window makes it difficult to read the result after 20 minutes (*see picture c*), or
- if any of the lines are NOT inside the "C" or "T" triangle areas (*see picture d1 and d2*)

An **Invalid** test result means that there was a problem running the test, either related to the specimen or to the Test Device. An **Invalid** result cannot be interpreted. **Repeat the test with a new Divided Pouch and a new oral fluid, fingerstick or venipuncture whole blood, or plasma sample. Contact OraSure Technologies' Customer Service if you are unable to get a valid test result upon repeat testing.**

LIMITATIONS OF THE TEST

1. The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test must be used in accordance with the instructions in this package insert to obtain an accurate result.
2. Reading test results earlier than 20 minutes or later than 40 minutes may yield erroneous results.
3. This test is approved by FDA for use with oral fluid, fingerstick whole blood, venipuncture whole blood, and plasma specimens only. Use of other types of specimens, testing of venipuncture whole blood specimens collected using a tube containing an anticoagulant other than EDTA, sodium heparin, sodium citrate, or ACD Solution A, or testing of plasma specimens collected using a tube containing an anticoagulant other than EDTA may not yield accurate results.
4. Individuals infected with HIV-1 or HIV-2 who are receiving highly active antiretroviral therapy (HAART) may produce false negative results.
5. Clinical data has not been collected to demonstrate the performance of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test in persons under 12 years of age.
6. A reactive result using the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test suggests the presence of HIV-1 and/or HIV-2 antibodies in the specimen. The OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test is intended as an aid in the diagnosis of infection with HIV-1 and/or HIV-2. AIDS and AIDS-related conditions are clinical syndromes and their diagnosis can only be established clinically.
7. For a reactive result, the intensity of the test line does not necessarily correlate with the titer of antibody in the specimen.
8. A non-reactive result does not preclude the possibility of exposure to HIV or infection with HIV. An antibody response to recent exposure may take several months to reach detectable levels.

PERFORMANCE CHARACTERISTICS

SENSITIVITY

DETECTION OF ANTIBODIES TO HIV-1 IN SPECIMENS FROM INDIVIDUALS INFECTED WITH HIV-1

ORAL FLUID
A sensitivity study was performed at eight clinical trial sites using freshly obtained oral fluid specimens collected from 767 individuals reported to be infected with HIV-1. Of the 767 specimens that were identified as seropositive using licensed confirmatory testing, 762 gave a reactive result on the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test. The results of this study are shown in Table 1.

A separate study was performed at four clinical trial sites using freshly obtained oral fluid specimens collected from 3150 previously unscreened individuals from populations at high risk for HIV-1 infection. The results of this study are also shown in Table 1. Of the 73 specimens that were identified as seropositive using licensed confirmatory testing, 72 were reactive using the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test.

TABLE 1
Detection of Antibody to HIV-1 in Oral Fluid Specimens from HIV-1 Seropositive Individuals

Test Group	Total Samples	OraQuick® *ADVANCE* Reactive	Licensed EIA Repeatedly Reactive	True Positive[1]
Known HIV-1 Positive	767	762	764	767
High-Risk	3150	72[2]	74[3]	73
TOTAL	3917	834	842	840

[1] Confirmation performed by licensed HIV-1 Western blot, with confirmation of indeterminate Western blot results by licensed immunofluorescence assay (IFA).
[2] Eight additional specimens were OraQuick® *ADVANCE* false positive (see Table 7).
[3] One specimen was EIA false positive, with a negative Western blot.

Combining the number of OraQuick® *ADVANCE* reactive results obtained from the study of confirmed positives with the number of OraQuick® *ADVANCE* reactive results obtained from the study of high-risk populations, the sensitivity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test in these studies was calculated to be 834/840 = 99.3% (95% C.I. = 98.4% - 99.7%).

PLASMA
A sensitivity study was performed at eleven clinical trial sites using EDTA-plasma specimens collected from 891 individuals reported to be infected with HIV-1. Of the 891 specimens that were identified as seropositive using licensed confirmatory testing, 887 gave a reactive result on the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test. The results of this study are shown in Table 2.

A separate study was performed at six clinical trial sites using EDTA-plasma specimens collected from 533 previously unscreened individuals from populations at high risk for HIV-1 infection. The results of this study are also shown in Table 2. All of the 14 specimens that were identified as seropositive using licensed confirmatory testing, were reactive using the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test.

TABLE 2
Detection of Antibody to HIV-1 in Plasma Specimens from HIV-1 Seropositive Individuals

Test Group	Total Samples	OraQuick® *ADVANCE* Reactive	Licensed EIA Repeatedly Reactive	True Positive[1]
Known HIV-1 Positive	891	887	891	891
High-Risk	553	14[2]	14	14
TOTAL	1424	901	905	905

[1] Confirmation performed by licensed HIV-1 Western blot, confirmation of indeterminate Western blot results by radioimmunoprecipitation assay (RIPA) or licensed IFA.
[2] One additional specimen was OraQuick® *ADVANCE* false positive (see Table 8).

Combining the number of OraQuick® *ADVANCE* reactive results obtained from the study of confirmed positives with the number of OraQuick® *ADVANCE* reactive results obtained from the study of high-risk populations, the sensitivity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test in these studies was calculated to be 901/905 = 99.6% (95% C.I. = 98.9% - 99.8%).

FINGERSTICK WHOLE BLOOD

A sensitivity study was performed at eight clinical trial sites using freshly obtained fingerstick whole blood samples from 481 individuals known to be infected with HIV-1 and 40 AIDS patients. Of the 521 specimens that were repeatedly reactive using a licensed EIA and positive by Western blot, 519 gave a reactive result on the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test. The results of this study are shown in Table 3.

A separate study was performed at seven clinical trial sites using 625 freshly obtained fingerstick whole blood samples from previously unscreened individuals from populations at high risk for HIV-1 infection. The results of this study are also shown in Table 3. Of the 625 specimens tested, 20 were repeatedly reactive using a licensed EIA, of which 17 were positive by Western blot. These same 17 specimens gave a reactive result using the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test.

TABLE 3
Detection of Antibody to HIV-1 in Fingerstick Whole Blood Samples from Patients with AIDS and from HIV-1 Seropositive Individuals

Test Group	Total Samples	OraQuick® *ADVANCE* Reactive	Licensed EIA Repeatedly Reactive	True Positive[1]
AIDS	40	40	40	40
Known HIV-1 Positive	481	479	481	481
High-Risk	625	17	20[2]	17
TOTAL	1146	536	541	538

[1] Confirmation performed by licensed HIV-1 Western blot, with confirmation of indeterminate Western blot results by RIPA.

[2] Two specimens were negative and one was indeterminate on Western blot with a negative RIPA.

Combining the number of OraQuick® *ADVANCE* reactive results obtained from the study of confirmed positives with the number of OraQuick® *ADVANCE* reactive results obtained from the study of high-risk populations, the sensitivity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test in these studies was calculated to be 536/538 = 99.6% (95% C.I. = 98.5% - 99.9%).

Reactivity with HIV-1 Specimens From Various Geographic Regions

To assess the sensitivity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test for HIV-1 variants from various geographic regions, 215 confirmed HIV-1 antibody-positive serum/plasma specimens were obtained from various parts of the world. Of these 215 specimens, 214 were reactive using the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test. One confirmed HIV-1 antibody-positive specimen from China was non-reactive using the OraQuick® *ADVANCE* test. An additional 13 specimens representing HIV-1 Subtypes A, B, C, D, F, and G, and Group O were tested and reactive on OraQuick® *ADVANCE*.

Reactivity with HIV-1 Seroconversion Panels

Eleven HIV-1 seroconversions panels were tested in comparison with licensed anti-HIV EIA tests. Each panel consisted of sequential serum/plasma specimens obtained from a single individual during seroconversion. The eleven seroconversion panels consisted of 69 specimens. The results of this study are shown in Table 4. In this study, the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test was demonstrated to be capable of detecting seroconversion similar to currently available FDA licensed EIAs.

TABLE 4
Comparison of the OraQuick® *ADVANCE* Rapid HtV-1/2 Antibody Test and Licensed Anti-HIV EIA Tests Using Seroconversion Panels

Specimen Information			Licensed Anti-HIV EIA Tests				
Panel	Relative Day of Bleed	OraQuick® *ADVANCE* Test	EIA #1	EIA #2	EIA #3	EIA #4	EIA #5
K	1	NR	NR	NR	NR	NR	NR
	7	NR	NR	NR	NR	NR	NR
	9	NR	NR	NR	NR	NR	NR
	14	R	NR	RR	NR	NR	NR
	16	R	NR	RR	NR	NR	NR
	21	R	NR	RR	NR	RR	RR
	23	R	RR	RR	RR	RR	RR
	30	R	RR	RR	RR	RR	RR
	34	R	RR	RR	RR	RR	RR
	37	R	RR	RR	RR	RR	RR
N	1	R	RR	RR	NR	NR	NR
	5	R	RR	RR	NR	RR	NR
	8	R	RR	RR	NR	RR	NR
	26	R	RR	RR	RR	RR	RR
	32	R	RR	RR	RR	RR	RR
Q	1	NR	NR	NR	NR	NR	NR
	54	NR	NR	NR	NR	NR	NR
	58	NR	NR	NR	NR	NR	NR
	61	NR	NR	RR	NR	NR	NR
	66	R	NR	RR	NR	NR	NR
	68	R	RR	RR	NR	NR	NR
	73	R	RR	RR	RR	RR	RR
R (M)	3	NR	NR	RR	NR	NR	NR
	8	NR	NR	RR	NR	NR	NR
	14	R	RR	RR	RR	RR	RR
	16	R	RR	RR	RR	RR	RR
	22	R	RR	RR	RR	RR	RR
S	1	NR	NR	NR	NR	NR	NR
	10	R	RR	RR	NR	NR	NR
	12	R	RR	RR	NR	RR	NR
W	1	NR	NR	NR	NR	NR	NR
	8	NR	NR	NR	NR	NR	NR
	13	NR	NR	NR	NR	NR	NR
	15	NR	NR	NR	NR	NR	NR
	29	NR	NR	NR	NR	NR	NR
	31	NR	NR	NR	NR	NR	NR
	36	NR	NR	NR	NR	NR	NR
	38	NR	NR	NR	NR	NR	NR
	48	NR	NR	RR	NR	NR	NR
	85	R	RR	RR	RR	RR	RR
	87	R	RR	RR	RR	RR	RR
	146	R	RR	RR	RR	RR	RR
	162	R	RR	RR	RR	RR	RR
AB	1	NR	NR	NR	NR	NR	NR
	29	NR	NR	RR	NR	NR	NR
	34	R	RR	RR	NR	NR	NR
	36	R	RR	RR	NR	NR	RR
	41	R	RR	RR	RR	RR	RR

Specimen Information			Licensed Anti-HIV EIA Tests				
Panel	Relative Day of Bleed	OraQuick® *ADVANCE* Test	EIA #1	EIA #2	EIA #3	EIA #4	EIA #5
AC	1	NR	NR	NR	NR	NR	NR
	112	NR	NR	RR	NR	NR	NR
	121	R	RR	RR	RR	RR	RR
	126	R	RR	RR	RR	RR	RR
	131	R	RR	RR	RR	RR	RR
AE	1	NR	NR	NR	NR	NR	NR
	4	NR	NR	NR	NR	NR	NR
	8	NR	NR	RR	NR	NR	NR
	11	NR	RR	RR	NR	RR	NR
AF	1	NR	NR	NR	NR	NR	NR
	3	NR	NR	NR	NR	NR	NR
	8	NR	NR	NR	NR	NR	NR
	10	NR	NR	NR	NR	NR	NR
	16	NR	NR	NR	NR	NR	NR
	29	R	NR	RR	NR	NR	NR
	34	R	RR	RR	NR	RR	RR
	36	R	RR	RR	RR	RR	RR
	43	R	RR	RR	RR	RR	RR
AI	1	NR	NR	NR	NR	NR	NR
	8	R	RR	RR	NR	NR	RR
	12	R	RR	RR	NR	RR	RR

NR = Non-Reactive; R = Reactive; RR = Repeatedly Reactive

Reactivity with HIV-1 Low Titer Panels

Two low titer HIV-1 antibody panels were tested in comparison with licensed anti-HIV EIA tests. The low titer antibody panels consisted of 30 serum/plasma specimens. The results of this study are shown in Table 5. In this study, the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test was demonstrated to be capable of detecting antibodies to HIV-1 similar to currently available FDA licensed EIAs.

TABLE 5
Comparison of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test and Licensed Anti-HIV EIA Tests Using Low Titer HIV-1 Antibody Panels

Specimen Information			Licensed Anti-HIV EIA Tests				
Panel	Member	OraQuick® *ADVANCE* Test	EIA #1	EIA #2	EIA #3	EIA #4	EIA #5
LT106	1	R	RR	RR	RR	RR	RR
	2	NR	NR	RR	NR	NR	NR
	3	R	RR	RR	RR	RR	RR
	4	R	RR	RR	RR	RR	RR
	5	R	RR	RR	RR	RR	RR
	6	NR	NR	NR	NR	NR	NR
	7	R	RR	RR	RR	RR	RR
	8	NR	RR	RR	NR	NR	NR
	9	R	RR	RR	RR	RR	RR
	10	R	RR	RR	RR	RR	RR
	11	R	RR	RR	NR	NR	RR
	12	R	RR	RR	NR	NR	RR
	13	R	RR	RR	RR	RR	RR
	14	R	RR	RR	RR	RR	RR
	15	R	RR	RR	RR	RR	RR

Specimen Information			Licensed Anti-HIV EIA Tests				
Panel	Member	OraQuick® *ADVANCE* Test	EIA #1	EIA #2	EIA #3	EIA #4	EIA #5
LT107	1	NR	NR	RR	RR	NR	NR
	2	R	NR	RR	RR	RR	NR
	3	R	NR	RR	NR	NR	NR
	4	R	RR	RR	RR	RR	NR
	5	NR	NR	NR	NR	NR	NR
	6	R	RR	RR	RR	RR	NR
	7	NR	NR	RR	RR	NR	NR
	8	NR	NR	RR	NR	RR	NR
	9	NR	NR	RR	NR	NR	NR
	10	R	RR	RR	RR	RR	RR
	11	R	RR	RR	RR	RR	RR
	12	NR	NR	RR	NR	NR	NR
	13	NR	NR	RR	RR	NR	NR
	14	R	RR	RR	RR	RR	RR
	15	R	RR	RR	RR	RR	RR

NR = Non-Reactive; R = Reactive; RR = Repeatedly Reactive

Interfering Substances and Unrelated Medical Conditions

To assess the impact of unrelated medical conditions or interfering substances on the sensitivity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test, 200 serum/plasma specimens from a variety of medical conditions unrelated to HIV-1 infection and 125 specimens with interfering substances were spiked with an HIV-1 positive specimen to give a level of reactivity in the low positive range (see list of medical conditions and interfering substances in Table 10 below). All spiked specimens gave reactive results.

In addition, a study was performed to assess the potential effect of anticoagulants on assay sensitivity. Venipuncture whole blood collected from 20 subjects, in each of 4 tubes containing one of four anticoagulants (EDTA, sodium heparin, sodium citrate, and ACD Solution A) was spiked with an HIV-1 positive specimen to give a level of reactivity in the low positive range. The samples were then aliquoted and stored either refrigerated (2°-8°C) or at room temperature (18°C) and tested over a 7-day period. There was no anticoagulant-specific effect observed on assay performance with samples held up to 30 hours at 2°-18°C.

As part of the oral fluid clinical studies, information was collected from the participants regarding concurrent diseases or medical conditions, oral pathologies, non-HIV viral infections, and other factors (e.g., use of tobacco products, mouthwash within 24 hours of testing, concomitant medications, dental fixtures, and food or drink immediately prior to testing). None of these disease states, medical conditions or other factors interfered with test sensitivity. In a separate study of 40 individuals, consumption of alcohol, brushing of teeth, use of mouthwash or smoking tobacco 5 minutes prior to testing, were shown to have no effect on test sensitivity.

DETECTION OF ANTIBODIES TO HIV-2 IN SPECIMENS FROM INDIVIDUALS INFECTED WITH HIV-2

A total of 324 serum/plasma specimens reported to be HIV-2 antibody positive were obtained from various repository sources. Specimens were tested by licensed anti-HIV-1/2 EIA, licensed anti-HIV-2 EIA, licensed HIV-1 Western blot, an HIV-2 Western blot and HIV-2 specific PCR. A total of 6 specimens were not demonstrated to be positive for antibodies to HIV-1 or HIV-2, all of which were OraQuick® *ADVANCE* non-reactive. Two of the 6 negative specimens were repeatedly reactive by licensed anti-HIV-1/2 EIA, negative by licensed anti-HIV-2 EIA, and indeterminate by licensed HIV-1 Western blot and by an HIV-2 Western blot.

Of the remaining 318 specimens, 151 were positive on an HIV-2 Western blot and 50 were positive using an HIV-2 specific PCR. One hundred and twenty-two specimens gave confirmatory results consistent with HIV-1 infection and were excluded from the analysis. One specimen was categorized as a dual infection based on additional testing by co-culture, and was not included in the sensitivity analysis. One specimen, while indeterminate on HIV-1 and HIV-2 Western blots, gave a positive result on an HIV-2 radioimmunoprecipitation assay (RIPA) and is also considered to be positive for antibodies to HIV-2. OraQuick® *ADVANCE* detected 201/201 (100%) of the specimens from individuals confirmed as positive for HIV-2 antibodies (see Table 6).

In a separate study, a total of 499 plasma specimens collected from an HIV-2 endemic area (Ivory Coast) were prepared as contrived whole blood and tested by OraQuick® *ADVANCE*, licensed anti-HIV-1/2 EIA, licensed anti-HIV-2 EIA, licensed HIV-1 Western blot, and an HIV-2 Western blot. Table 6 shows a summary of the results. OraQuick® *ADVANCE* was reactive with all of the 27 specimens that were repeatedly reactive by licensed anti-HIV-1/2 EIA, licensed anti-HIV-2 EIA and positive on licensed HIV-1 Western blot, and with all three specimens that were confirmed as positive for HIV-2 only by an HIV-2 Western blot. Two specimens were OraQuick® *ADVANCE* false positive.

TABLE 6
Detection of Antibody to HIV-2 in Samples from HIV-2 Seropositive Individuals and Individuals at High Risk of HIV-2 Infection

Test Group	Total Samples	OraQuick® *ADVANCE* Reactive	Licensed anti-HIV-2 EIA Repeatedly Reactive or HIV-2 PCR Positive	True HIV-2 Positive[1]
Known HIV-2 Positive	324[2]	201	201[3]	201[4]
High-Risk	499	32	33	3
TOTAL	823	233	234	204

[1] Confirmation performed by HIV-2 Western blot, with RIPA confirmation of Indeterminate Western blot results.
[2] One hundred and twenty-two specimens gave confirmatory results consistent with HIV-1 infection and were excluded from the analysis. In addition, one specimen was categorized as a dual infection based on additional testing by co-culture, and was not included in the sensitivity analysis.
[3] 151 specimens were tested with an anti-HIV-2 EIA alone. HIV-2 DNA or RNA PCR was performed on the remaining 50 specimens instead of EIA. All results were positive.
[4] One specimen was confirmed to be HIV-2 positive based on the positive results of an HIV-2 specific RIPA.

Combining the number of OraQuick® *ADVANCE* reactive results obtained from the study of confirmed positives with the number of OraQuick® *ADVANCE* reactive results obtained from the study of the high risk population, the sensitivity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test for the detection of antibodies to HIV-2 in these studies was calculated to be 204/204 = 100% (95% C.I. = 98.2% - 100%).

In addition, 3 HIV-2 infected individuals located in the USA were tested by fingerstick whole blood and oral fluid OraQuick® *ADVANCE* tests. Fingerstick whole blood and oral fluid samples from all three subjects were reactive on the OraQuick® *ADVANCE* test.

SPECIFICITY

ORAL FLUID

A specificity study was performed at four clinical trial sites using freshly obtained oral fluid specimens collected from 605 previously unscreened individuals at low risk for HIV-1 infection. All of the 605 specimens were correctly non-reactive using the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test. Of the 3077 HIV antibody-negative specimens from the four study sites that examined populations at high risk for HIV-1 infection, the OraQuick® *ADVANCE* test was non-reactive for 3069. The results are summarized in Table 7.

TABLE 7
Performance of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test on Oral Fluid Specimens from Individuals Presumed to be Negative for HIV Infection

Test Group	Total Samples	OraQuick® *ADVANCE* Non-Reactive	Licensed EIA Non-Reactive	True Negative[1]
Low-Risk	605	605	599[2]	605
High-Risk	3150	3069[3]	3076[4]	3077
TOTAL	3755	3674	3675	3682

[1] Confirmation performed by licensed HIV-1 Western blot, with confirmation of indeterminate Western blot results by RIPA or IFA.
[2] Six specimens were EIA false positive, five with a negative Western blot and one with an indeterminate blot which was confirmed negative by IFA.
[3] One additional specimen was OraQuick® *ADVANCE* false negative (see Table 1).
[4] One specimen was EIA false positive with a negative Western blot.

Combining the number of OraQuick® *ADVANCE* non-reactive results obtained from the study of the low-risk populations with the number of OraQuick® *ADVANCE* non-reactive results obtained from the study of the high-risk populations, the specificity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test in these studies was calculated to be 3674/3682 = 99.8% (95% C.I. = 99.6% - 99.9%).

PLASMA

A specificity study was performed at seven clinical trial sites using EDTA-plasma specimens collected from 1102 previously unscreened individuals at low risk for HIV infection. All of the specimens, except for one, gave non-reactive results using the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test. In addition, 519 of the 520 HIV antibody-negative specimens from study sites that examined populations at high risk for HIV-1 infection also gave non-reactive results using the OraQuick® *ADVANCE* test. The results of this study are shown in Table 8.

TABLE 8
Performance of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test on Plasma Specimens from Individuals Presumed to be Negative for HIV Infection

Test Group	Total Samples	OraQuick® *ADVANCE* Non-Reactive	Licensed EIA Non-Reactive	True Negative[1]
Low-Risk	1102	1101	1096[2]	1102
High-Risk	534	519	516[3]	520
TOTAL	1636	1620	1612	1622

[1] Confirmation performed by licensed HIV-1 Western blot, with confirmation of indeterminate Western blot results by RIPA or IFA.
[2] Six specimens were EIA false positive, five with a negative Western blot and one with an indeterminate blot which was confirmed negative by IFA
[3] Four specimens were EIA false positive, with 1 negative and 3 indeterminate by Western blot, that confirmed negative by IFA.

Combining the number of OraQuick® *ADVANCE* non-reactive results obtained from the study of the low-risk populations with the number of OraQuick® *ADVANCE* non-reactive results obtained from the study of the high-risk populations, the specificity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test in these studies was calculated to be 1620/1622 = 99.9% (95% C.I. = 99.6% - 99.9%).

FINGERSTICK WHOLE BLOOD

A specificity study was performed at eight clinical trial sites using freshly obtained fingerstick whole blood samples from 1250 previously unscreened individuals at low risk for HIV-1 infection. In the course of this study, two specimens were confirmed to have antibodies to HIV-1 and were removed from the specificity calculation. All of the remaining specimens gave non-reactive results using the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test. In addition, all of the 608 HIV-1 antibody-negative specimens from the study sites that examined populations at high risk for HIV-1 infection also gave non-reactive results using the OraQuick® *ADVANCE* test. The results of this study are shown in Table 9.

TABLE 9
Performance of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test on Fingerstick Whole Blood Specimens from Individuals Presumed to be Negative for HIV Infection

Test Group	Total Samples	OraQuick® *ADVANCE* Non-Reactive	Licensed EIA Non-Reactive	True Negative[3]
Low-Risk	1250[1]	1248	1247[2]	1248
High-Risk	625	608	605	608
TOTAL	1875	1856	1853	1856

[1] Two specimens in the low-risk study that gave reactive results using the OraQuick® *ADVANCE* test, repeatedly reactive results using a licensed EIA, and positive results using a licensed Western blot were removed from the calculation of specificity.
[2] One specimen was EIA repeatedly reactive, Western blot negative.
[3] True negative status based on negative or indeterminate test results using a licensed Western blot.

Combining the number of OraQuick® *ADVANCE* non-reactive results obtained from the study of the low-risk populations with the number of OraQuick® *ADVANCE* non-reactive results obtained from the study of the high-risk populations, the specificity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test in these studies was calculated to be 1856/1856 = 100% (95% C.I. = 99.7% - 100%).

INTERFERING SUBSTANCES AND UNRELATED MEDICAL CONDITIONS

To assess the impact of unrelated medical conditions or interfering substances on the specificity of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test, 321 serum/plasma specimens from a variety of medical conditions unrelated to HIV infection and 119 specimens with interfering substances were analyzed. The results of this study are shown in Table 10. One specimen from subjects known to be positive for EBV, for HBV, or for rheumatoid factor, one from a multiparous woman, and three specimens from known HAV infected subjects gave false positive results.

In addition, a study was performed to assess the potential effect of anticoagulants on assay specificity. Venipuncture whole blood was collected from 20 HIV negative subjects, in each of 4 tubes containing one of the following anticoagulants: EDTA, sodium heparin, sodium citrate, and ACD Solution A. The samples were then aliquoted and stored either refrigerated (2°-8°C) or at room

temperature (18°C) and tested over a 7-day period. There was no anticoagulant-specific effect observed on assay performance with samples held up to 30 hours at 2°-18°C (refer to Table 10).

TABLE 10

OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test Reactivity with Specimens from Individuals with Potentially Interfering Medical Conditions and Specimens with Interfering Substances

	OraQuick® *ADVANCE* Results	
Medical Condition (n = 321)	Reactive	Non-Reactive
Multiparous women	1 [2]	14
Anti-nuclear antibody (ANA)	0	17
Lupus	0	15
Rheumatoid factor	1 [2]	17
Cytomegalovirus (CMV)	0	15
Epstein Barr virus (EBV)	1 [2]	14
Hepatitis A virus (HAV)	3 [1]	17
Hepatitis B virus (HBV)	1 [2]	16
Hepatitis C virus (HCV)	0	15
Human T-cell Lymphotropic virus Type I (HTLV-I)	0	15
Human T-cell Lymphotropic virus Type II (HTLV-II)	0	15
Rubella	0	15
IgG gammopathies	0	13
IgM gammopathies	0	12
Syphilis	0	15
Toxoplasmosis	0	15
Tuberculosis	0	15
Influenza	0	10
Multiple transfusions	0	10
Hemophiliac	0	10
Herpes Simplex virus	0	5
Cirrhosis	0	5
Dialysis patient	0	4
Colon cancer	0	4
HTLV I/II	0	2
Chlamydia	0	3
Anti-scl or anti-rnp antibody	0	3
Breast cancer	0	1
Anti-DNA antibody	0	1
Gonorrhea	0	1
Interfering Substances (n = 199)		
Elevated Bilirubin	0	20
Elevated Hemoglobin	0	20
Elevated Triglycerides	0	20
Elevated Protein	0	20
Bacterially Contaminated	0	25
Visual Hemolysis (hemolytic)	0	5
Icteric	0	5
Lipemic	0	4
Sodium Heparin[3]	0	20
EDTA[3]	0	20
Sodium Citrate[3]	0	20
ACD Solution A[3]	0	20

[1] A total of 3 of the 20 HAV specimens were OraQuick® *ADVANCE* falsely reactive. Two of the 3 specimens were OraQuick® *ADVANCE* non-reactive at the 20-25 minute read time and reactive at the 55-60 minute read time. The remaining specimen was reactive at both read times.

[2] One of the specimens was OraQuick® *ADVANCE* non-reactive at the 20-25 minute read time and reactive at the 55-60 minute read time.

[3] The OraQuick® *ADVANCE* assay maximum read time for these specimens was 40 minutes.

As part of the oral fluid clinical studies, information was collected from the participants regarding concurrent diseases or medical conditions, oral pathologies, non-HIV viral infections, and other factors (e.g., use of tobacco products, mouthwash within 24 hours of testing, concomitant medications, dental fixtures, and food or drink immediately prior to testing). None of these disease states, medical conditions or other factors interfered with test specificity. In a separate study of 40 individuals, consumption of alcohol, brushing of teeth, use of mouthwash or smoking tobacco 5 minutes prior to testing, were shown to have no effect on test specificity.

REPRODUCIBILITY

The reproducibility of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test was tested at 3 sites using 3 lots of the device on 3 different days with 9 operators (3 per site). A blind-coded panel was tested that consisted of 5 contrived blood specimens (4 antibody-positive and 1 antibody-negative). Test results were recorded at 20-25 minutes and at 55-60 minutes. A total of 405 tests were performed (135/site), with a total of 81 tests per panel member. The overall reproducibility of the OraQuick® *ADVANCE* Rapid HIV-1/2 Antibody Test was 405/405 = 100%. Concordance between the specified assay read time limits was 99.8% (404/405); a single HIV-1 low positive panel member that was non-reactive at the 20-25 minute read time was reactive at the 55-60 minute read time.

RESULTS OF UNTRAINED USER STUDY

An "Untrained User" study was conducted in which participants were given only the test instructions and asked to perform testing of a blinded panel comprised of 6 randomized specimens of three different levels (Negative, Low Positive and High Positive OraQuick® *ADVANCE* test reactivity) consisting of human plasma. The participants were not given any training on the use of the test or the interpretation of the test results, nor were they allowed to observe the performance of the Kit Controls by the Study Coordinator. The study protocol stipulated that professionally trained medical laboratory personnel or persons with prior experience using the OraQuick® *ADVANCE* device were excluded from participation. A total of 100 participants were enrolled from a total of four sites, representing a diverse demographic (educational, ethnic, age, gender, etc.) population.

The rate of correct results for the overall study was 98.6% (592/600). Refer to the table below for a summary of the performance relative to the specimen type. The eight incorrect results were attributed to six participants. Of these six participants, four obtained 5 out of 6 correct results, and two participants obtained 4 out of 6 correct results.

Untrained Users Rate of Correct Test Results			
Negative	Low Positive	High Positive	Total
98.5% (197/200) 95% C.I. (95.7% - 99.7%)	98.0% (196/200) 95% C.I. (95.0% - 99.5%)	99.5% (199/200) 95% C.I. (97.3% - 99.9%)	98.6% (592/600) 95% C.I. (97.4% - 99.4%)

There were 1.7% (10/600) Invalid results reported, with 5 of the 10 Invalid results attributed to one participant. All tests were successfully repeated, with 8/10 of the repeat test results interpreted correctly. The 2 incorrect repeat results were attributed to one participant. As part of the Untrained User study, a Participant Feedback Questionnaire was completed. All participants rated the test as 'easy to use' and felt 'able to perform the test correctly'.

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